Use of donor semen in the treatment of male infertility

Where is the evidence?

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Strength of evidence

Systematic review	1A
Meta-analysis	1A
RCT	1B
Well designed non-randomized controlled trial	2A
Well designed quasi experimental	2B
Descriptive / cases	3
Expert	4

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Intra-Uterine versus Intra-Cervical 1A

Goldberg et al., Fertil. Steril., 1999;72(5):792-795

Comparison of intrauterine and intracervical insemination with frozen donor sperm: a meta-analysis

IUI is superior over ICI: The pooled OR was 2.4

95% CI: 1.5- 3.8

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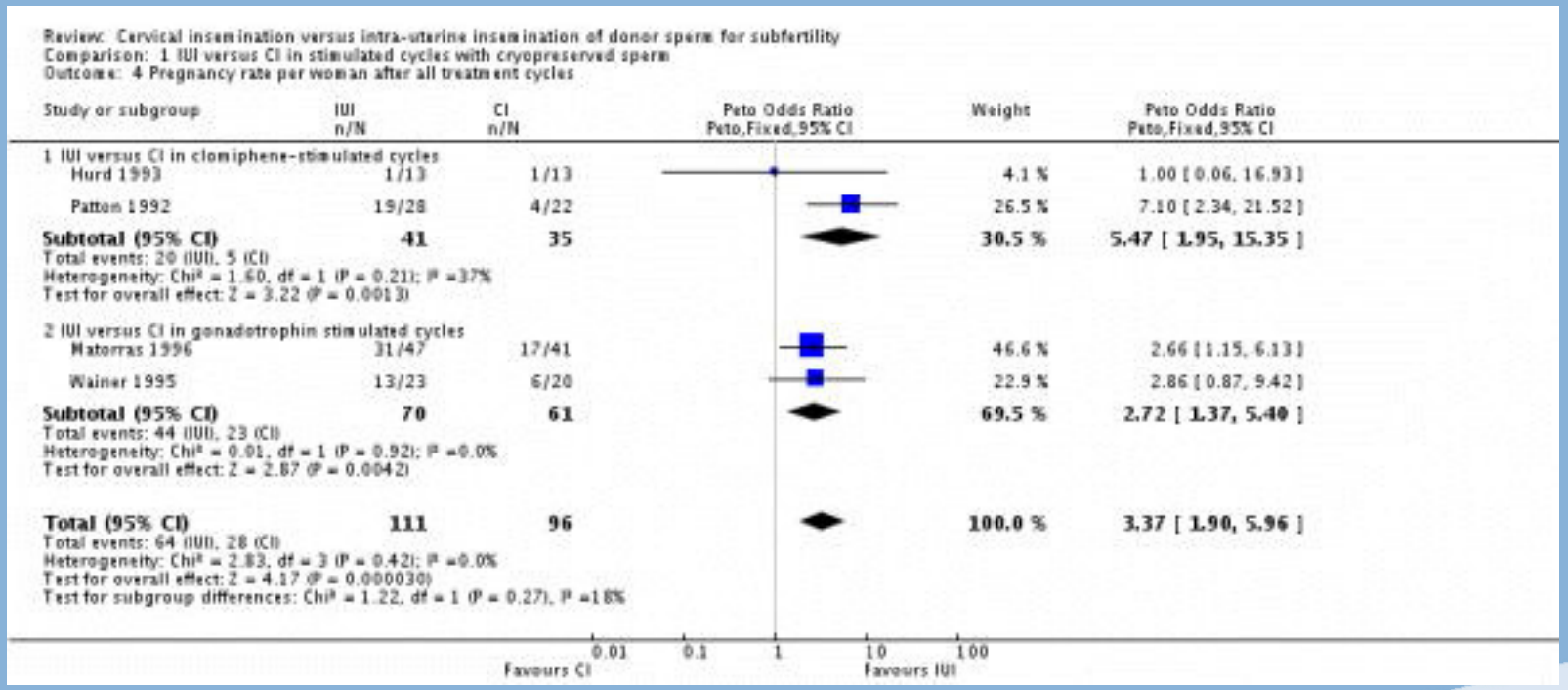
Intra-Uterine versus Intra-Cervical 1A

Besselink et al., Cochrane Database of Systematic Reviews, 2, 2009

Cervical insemination versus intra-uterine insemination of donor sperm for subfertility



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Intra-Uterine versus Intra-Cervical 1A

Besselink et al., Cochrane Database of Systematic Reviews, 2, 2009

Cervical insemination versus intra-uterine insemination of donor sperm for subfertility

IUI is superior to ICI in terms of:

Pregnancy rate

Live birth rate

With no difference in:

Miscarriage rate

Multiple pregnancies

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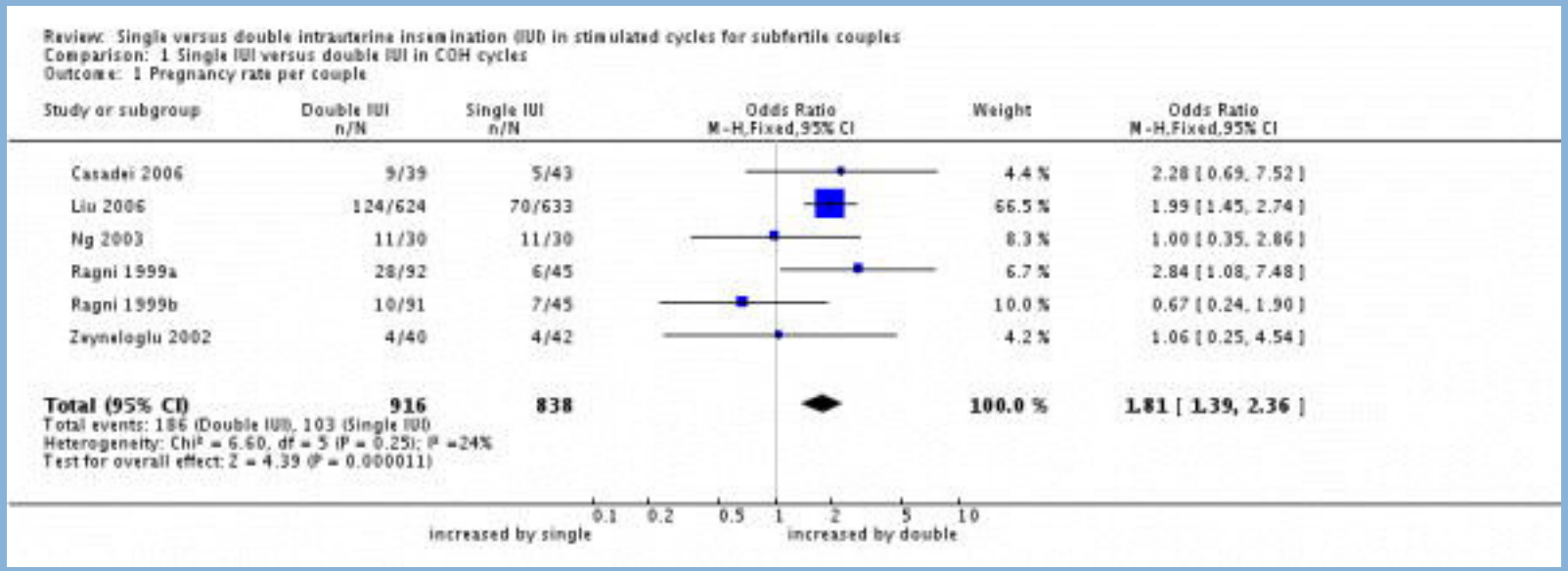
Single or double insemination

1A

Cantineau et al., *Cochrane Database of Systematic Reviews*, 2, 2009

Single versus double intrauterine insemination (IUI) in stimulated cycles for subfertile couples



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Single or double insemination

1A

Cantineau et al., *Cochrane Database of Systematic Reviews*, 2, 2009

Single versus double intrauterine insemination (IUI) in stimulated cycles for subfertile couples

Note: fresh partner semen

IUI performed on consequetive days is superior over a single insemination

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Single or double insemination

2A

Matilsky et al., J Androl., 1998; 19(5):603-7

Two-day IUI treatment cycles are more successful than one-day IUI cycles when using frozen-thawed donor sperm

PR 5% per cycle after single insemination

9.7% per patient

PR 17.9 per cycle after double insemination

37.9% per patient

The results of this study support the use of 2-day IUI treatment cycles when using frozen-thawed donor sperm.

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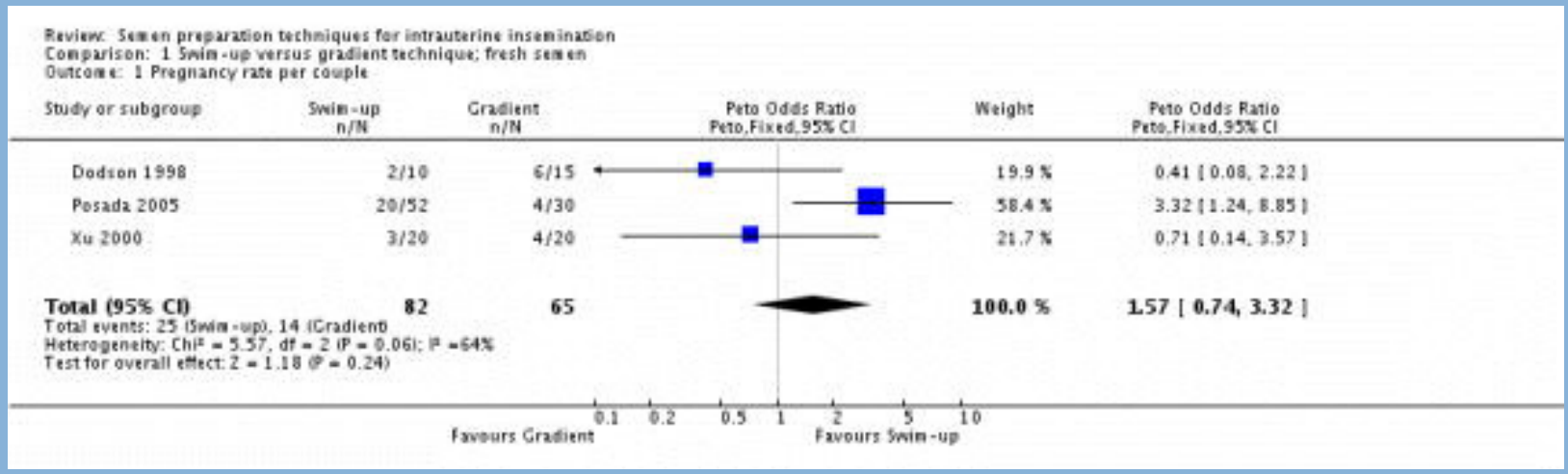
Swim-up versus gradient

1A

Boomsma et al., Cochrane Database of Systematic Reviews, 2, 2009

Semen preparation techniques for intrauterine insemination



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Swim-up versus gradient

1A

Boomsma et al., Cochrane Database of Systematic Reviews, 2, 2009

Semen preparation techniques for intrauterine insemination

Note: fresh partner semen

No evidence of a difference between either swim-up, gradient or wash and centrifugation was observed.

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Number of motile spermatozoa to inseminate 1A

Van Weert et al., Fertil Steril., 2004; 82(3):612-20

Performance of the postwash total motile sperm count as a predictor of pregnancy at the time of intrauterine insemination: a meta-analysis

Note: fresh partner semen

- at cut-off levels between 0.8 to 5 million motile spermatozoa, the postwash TMC provided a substantial discriminative performance
- the cut-off value for a postwash TMC during the fertility workup should be based on the clinic's own population and sperm-preparation technique

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Number of motile spermatozoa to inseminate 2B

Curfs, unpublished results

Number of motile spermatozoa:

≤ 1 million	PR 11,8%	OPR 8,6%
>1 and ≤ 2 million	PR 13,7%	OPR 11,6%
>2 million	PR 14,1%	OPR 9,6%

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Fresh versus frozen

2B

Keel and Webster, Ferti. Steril., 1989; 52(1):100-5

Semen analysis data from fresh and cryopreserved donor ejaculates: comparison of cryoprotectants and pregnancy rates.

the number of motile sperm of cryopreserved ejaculates are dramatically reduced compared with the fresh counterparts

if a minimum criteria for ejaculate quality is established, the use of cryopreserved semen can offer a viable, effective, and relatively safe alternative to artificial insemination by donor with fresh semen

Low patient numbers

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Fresh versus frozen

Feldschuh et al., Fertil Steril., 2005; 84(4):1017

Successful sperm storage for 28 years.

Artificial insemination with semen cryopreserved for 21 and 28 years resulted in two live births.

Fresh versus frozen

COMMISSION DIRECTIVE 2006/17/EC of 31 March 2004

implementing Directive 2004/23/EC …. as regards certain technical requirements for the …. testing of human tissues and cells

Annex III, 4.3: Sperm donations other than by partners will be quarantined for a minimum of 180 days, after which repeat testing is required.

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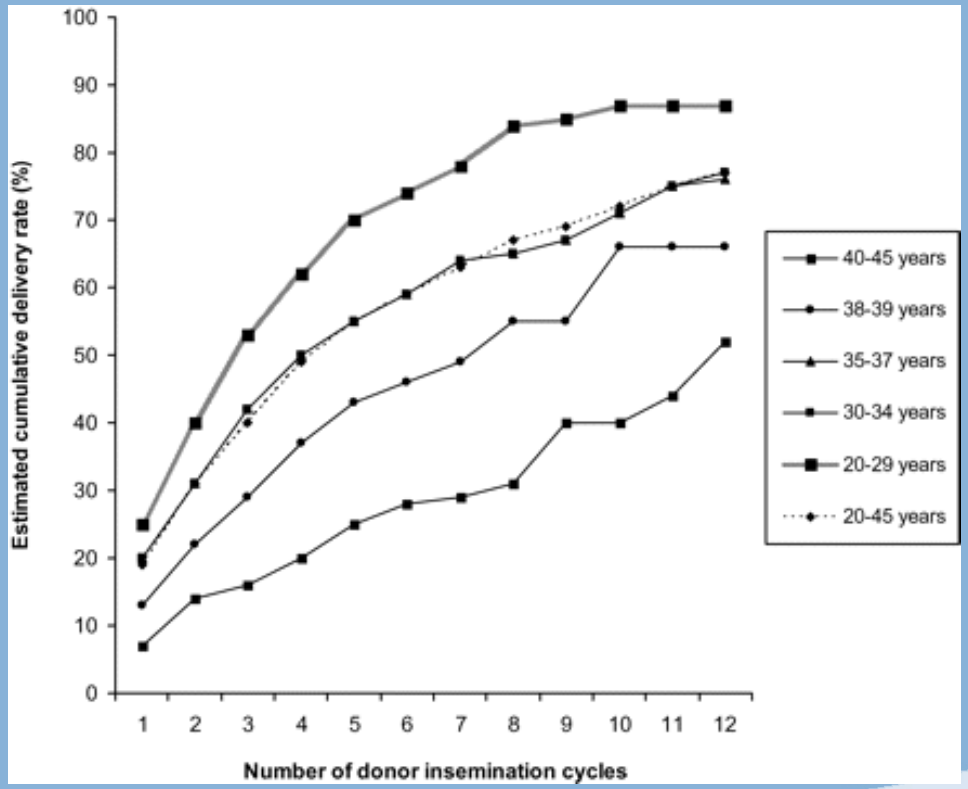
Number of treatment cycles?

2B

De Brucker et al., Hum. Reprod., 2009; 24(8):1891-1899

Cumulative delivery rates in different age groups after artificial insemination with donor sperm



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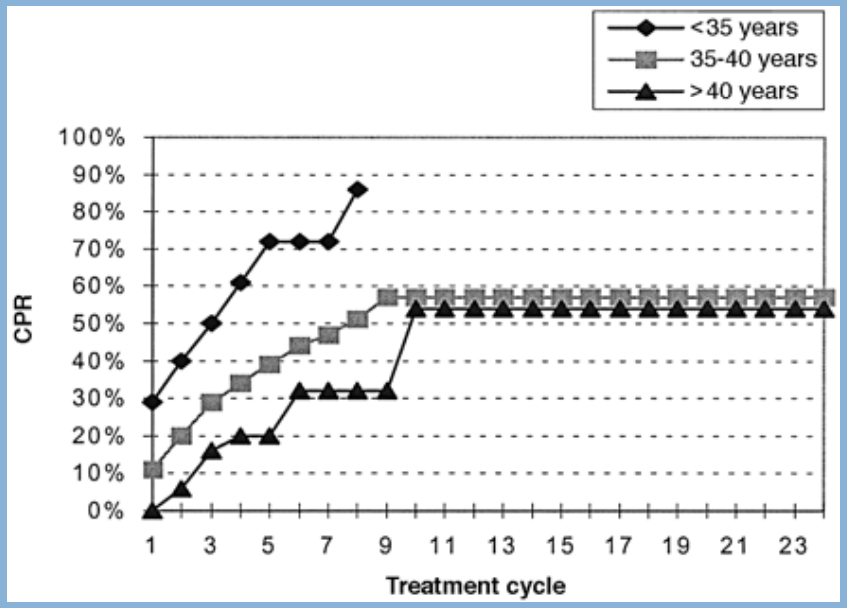
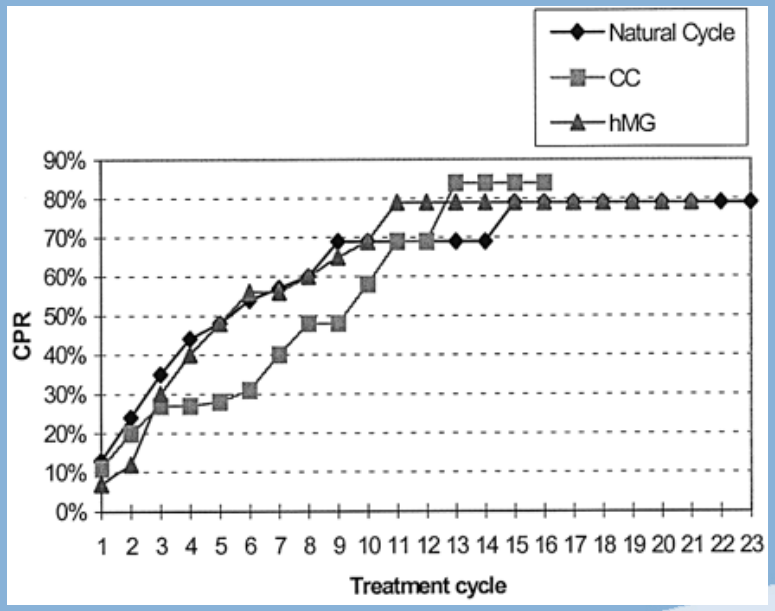
Number of treatment cycles?

2B

Ferrara et al., Hum. Reprod., 2002; 17(9):2320-4

Intrauterine insemination with frozen donor sperm. Pregnancy outcome in relation to age and ovarian stimulation regime





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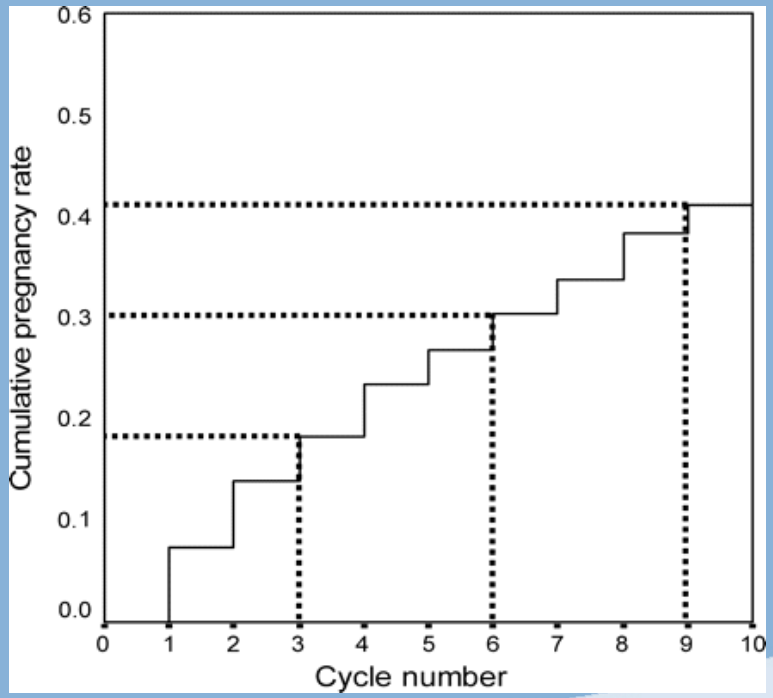
Number of treatment cycles?

2B

Custers et al., Hum. Reprod., 2008; 23(4):885-888

Intrauterine insemination: how many cycles should we perform?

Note: fresh partner semen



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Time to inseminate

2B

Yavas and Selub, Fertil. Steril., 2004; 82(6):1638-47

Intrauterine insemination (IUI) pregnancy outcome is enhanced by shorter intervals from semen collection to sperm wash, from sperm wash to IUI time, and from semen collection to IUI time

Note: fresh partner semen

TABLE 2

Comparison of intervals for semen specimens collected at home or at the clinic for IUI and comparison of intervals for semen specimens between IUI cycles that resulted in pregnancy and IUI cycles that did not result in pregnancy in CC- and hMG-treated women, irrespective of semen collection place.

	Semen collection place			CC–Pregnant			hMG–Pregnant		
Variable	Home	Clinic	*P*	No	Yes	*P*	No	Yes	*P*
C-SW[a]	45 ± 2	19 ± 1	<.0001	38 ± 2	28 ± 4	.19	41 ± 3	27 ± 4	.01
SW-IUI[a]	70 ± 7	51 ± 10	.15	63 ± 8	51 ± 11	.40	85 ± 12	42 ± 5	.003
C-IUI[a]	145 ± 8	100 ± 10	.001	131 ± 9	109 ± 14	.45	156 ± 13	99 ± 7	.0006
n	71	31	—	67	6	—	21	8	—

Note: CC = clomiphene citrate; C-SW = interval from semen collection to start of sperm wash; SW-IUI = interval from end of sperm wash to IUI; C-IUI = interval from semen collection to IUI.

[a] Intervals in minutes; mean ± SEM.

Yavas. Prompt sperm wash enhances IUI pregnancy. Fertil Steril 2004.

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Time to inseminate

2B

Song et al., **Fertil. Steril., 2007;** 88 (6), 1689-1691

Location of semen collection and time interval from collection to use for intrauterine insemination

Note: fresh partner semen

TABLE 1

Semen values and time intervals from semen collection to insemination of intrauterine insemination (IUI) cycles (mean ± SD) in the groups with clinic versus home collection of semen or in the pregnant versus nonpregnant groups.

	Collection place		Pregnancy	
	Clinic (n = 397)	Home (n = 236)	Pregnant (n = 88)	Nonpregnant (n = 545)
Age of female patient (years)	34 ± 4.3	35 ± 4.9[a]	34 ± 4.7	34 ± 4.9
Semen parameters				
Sperm count (million/mL)	59 ± 40	58 ± 40	65 ± 43	58 ± 40
Sperm motility (%)	44 ± 19	41 ± 17	45 ± 20	43 ± 18
Progressive (velocity)	31 ± 7	30 ±7[a]	32 ± 7	30 ± 7
Total motile sperm (million)	81 ± 84	67 ± 73	88 ± 93	71 ± 75
Time intervals (min)				
Collection to washing	14 ± 8	29 ± 15[a]	20 ± 11	20 ± 13
Washing to insemination	21 ± 14	18 ± 11[a]	18 ± 12	20 ± 13
Collection to insemination	69 ± 15	81 ± 20[a]	70 ± 19	73 ± 18
Ongoing pregnancy rate	7.3% (29/397)	10.6% (25/236)		

[a] *P* value <.05; n = the number of cycles.

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Time to inseminate

2B

Curfs, unpublished results

Retrospective analysis, 1796 cycles

Interval from gradient centrifugation to insemination			
	Pregnant	Total	Pregnancy rate
<3 h	66	592	11,1
>3 h	101	1204	8,4
			p<0,05

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Conclusions

- There is strong evidence that Intra Uterine Insemination is superior to Intra Cervical Insemination
- There is evidence that a double insemination on consequetive days is superior to a single insemination
- The evidence is inconclusive to which method is optimal for processing semen (after thawing)
- There is evidence that the minimal number of motile sperm to inseminate is between 0,8 and 5 million. However, each laboratory should determine its own cut-off level
- There is no evidence that fresh semen yields better results than frozen-thawed semen. European legislation prohibits the use of fresh donorsemen

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Conclusions

- There is no evidence of decreased pregnacy rates up until 8-12 cycles
- There is evidence that increasing the interval from sperm processing to insemination results in decreased pregnancy rates

- We need more and stronger data on almost every aspect of the treatment with donorsperm [4]

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